PATENT COOPERATION TREATY

From the
INTERNATIONAL SEARCHING AUTHORITY

To:

see form PCT/ISA/220

PCT

WRITTEN OPINION OF THE INTERNATIONAL SEARCHING AUTHORITY

(PCT Rule 43*bis*.1)

Date of mailing *(day/month/year)* see form PCT/ISA/210 (second sheet)	
Applicant's or agent's file reference see form PCT/ISA/220	**FOR FURTHER ACTION** See paragraph 2 below

International application No.	International filing date *(day/month/year)*	Priority date *(day/month/year)*
PCT/CZ2005/000019	15.02.2005	20.02.2004

International Patent Classification (IPC) or both national classification and IPC
A61K47/48, A61K31/19

Applicant
I.Q.A., A.S.

1. This opinion contains indications relating to the following items:

- ☒ Box No. I Basis of the opinion
- ☐ Box No. II Priority
- ☐ Box No. III Non-establishment of opinion with regard to novelty, inventive step and industrial applicability
- ☐ Box No. IV Lack of unity of invention
- ☒ Box No. V Reasoned statement under Rule 43*bis*.1(a)(i) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement
- ☐ Box No. VI Certain documents cited
- ☒ Box No. VII Certain defects in the international application
- ☐ Box No. VIII Certain observations on the international application

2. **FURTHER ACTION**

If a demand for international preliminary examination is made, this opinion will usually be considered to be a written opinion of the International Preliminary Examining Authority ("IPEA"). However, this does not apply where the applicant chooses an Authority other than this one to be the IPEA and the chosen IPEA has notifed the International Bureau under Rule 66.1*bis*(b) that written opinions of this International Searching Authority will not be so considered.

If this opinion is, as provided above, considered to be a written opinion of the IPEA, the applicant is invited to submit to the IPEA a written reply together, where appropriate, with amendments, before the expiration of three months from the date of mailing of Form PCT/ISA/220 or before the expiration of 22 months from the priority date, whichever expires later.

For further options, see Form PCT/ISA/220.

3. For further details, see notes to Form PCT/ISA/220.

Name and mailing address of the ISA:	Authorized Officer
European Patent Office D-80298 Munich Tel. +49 89 2399 - 0 Tx: 523656 epmu d Fax: +49 89 2399 - 4465	Hedegaard, A Telephone No. +49 89 2399-8644

10/588870

WRITTEN OPINION OF THE INTERNATIONAL SEARCHING AUTHORITY

International application No.
PCT/CZ2005/000019

IAP20 Rec'd PCT/PTO 10 AUG 2006

Box No. I Basis of the opinion

1. With regard to the **language**, this opinion has been established on the basis of the international application in the language in which it was filed, unless otherwise indicated under this item.

   ☐ This opinion has been established on the basis of a translation from the original language into the following language , which is the language of a translation furnished for the purposes of international search (under Rules 12.3 and 23.1(b)).

2. With regard to any **nucleotide and/or amino acid sequence** disclosed in the international application and necessary to the claimed invention, this opinion has been established on the basis of:

   a. type of material:

   ☐ a sequence listing

   ☐ table(s) related to the sequence listing

   b. format of material:

   ☐ in written format

   ☐ in computer readable form

   c. time of filing/furnishing:

   ☐ contained in the international application as filed.

   ☐ filed together with the international application in computer readable form.

   ☐ furnished subsequently to this Authority for the purposes of search.

3. ☐ In addition, in the case that more than one version or copy of a sequence listing and/or table relating thereto has been filed or furnished, the required statements that the information in the subsequent or additional copies is identical to that in the application as filed or does not go beyond the application as filed, as appropriate, were furnished.

4. Additional comments:

Box No. V Reasoned statement under Rule 43*bis*.1(a)(i) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

1. Statement

Novelty (N)	Yes:	Claims	1-10
	No:	Claims	
Inventive step (IS)	Yes:	Claims	
	No:	Claims	1-10
Industrial applicability (IA)	Yes:	Claims	1-10
	No:	Claims	

2. Citations and explanations

see separate sheet

Box No. VII Certain defects in the international application

The following defects in the form or contents of the international application have been noted:

see separate sheet

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JAP20 Rec'd PCT/PTO 10 AUG 2006

WRITTEN OPINION OF THE INTERNATIONAL SEARCHING AUTHORITY (SEPARATE SHEET)

International application No.
PCT/CZ2005/000019

Re Section V

Reasoned statement under Rule 66.2(a)(ii) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

1. Reference is made to the following documents:

   D1: EP-A-0 490 193
   D2: US-A-5 024 997

   D1 (see claims 1, 11 and 20) discloses complexes of S(+)-ibuprofen and hydroxypropyl beta-cyclodextrin in a weight ratio of 0,01 - 2,0. Said complexes can be used in syrups (see claim 34). Example 10 of D1 discloses a syrup comprising a complex of S(+)-ibuprofen and dimethyl beta-cyclodextrin; and sweetener.

   D2 (see the examples) discloses syrups comprising ibuprofen, hydroxypropyl beta-cyclodextrin and sweetener.

2. Novelty (Art. 33(2) PCT):

   The subject-matter of claims 1-3 (syrup) and 4-10 (method) is novel since a syrup comprising S(+)-ibuprofen, hydroxypropyl beta-cyclodextrin and at least one sweetener in the defined amounts has not been disclosed in the available prior art documents.

3. Inventive step (Art. 33(3) PCT):

3.1 The problem of the present application was to provide stable palatable syrups containing ibuprofen. This problem is solved by the syrup according to present claim 1 wherein S(+)-ibuprofen is combined with hydroxypropyl beta-cyclodextrin.

However, D1 has already disclosed that complexes of S(+)-ibuprofen and beta-cyclodextrin (e.g. hydroxypropyl-beta-cyclodextrin) have better dissolution and

bioavailability characteristics (D1, p. 3, l. 19-20 and p. 4, l. 15-17) and can be used in syrups (D1, claim 34).

The subject-matter of present claim 1 only differs from that of D1 in specifying the presence of sweetener. However, this minor amendment appears to be trivial for the skilled person and can be carried out without having to resort to inventive skill, in particular since example 10 of D1 already discloses the presence of sweetener in such syrups.

Therefore, the subject-matter of claim 1 is not considered to involve an inventive step over D1.

3.2 Also a combination of D2 with D1 appears to destroy inventive step for the following reason:

The subject-matter of present claim 1 only differs from the examples of D2 in specifying that the S(+)-form is used. However, in view of D1, which discloses the better solubility and bioavailability characteristics of the S(+)-complex, it seems to be obvious for the skilled person, faced with the above-mentioned problem, to include the S(+)-form known from D1 in the compositions of D2 and thus, to arrive at the subject-matter of present claim 1.

4. Having regard to the disclosures of D1 and D2, dependent claims 2-3 and method claims 4-10 do not appear to contain inventive features and are only allowable when related to an independent claim which fulfils the requirements of the PCT.

Re Section VII

Certain defects in the international application

1. Contrary to the requirements of Rule 5.1(a)(ii) PCT, the relevant background art

disclosed in the document D1 is not mentioned in the description, nor is this document identified therein.